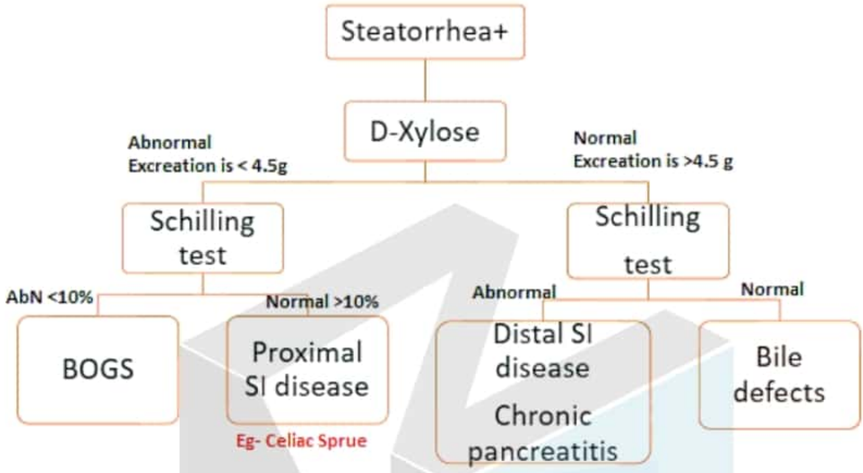
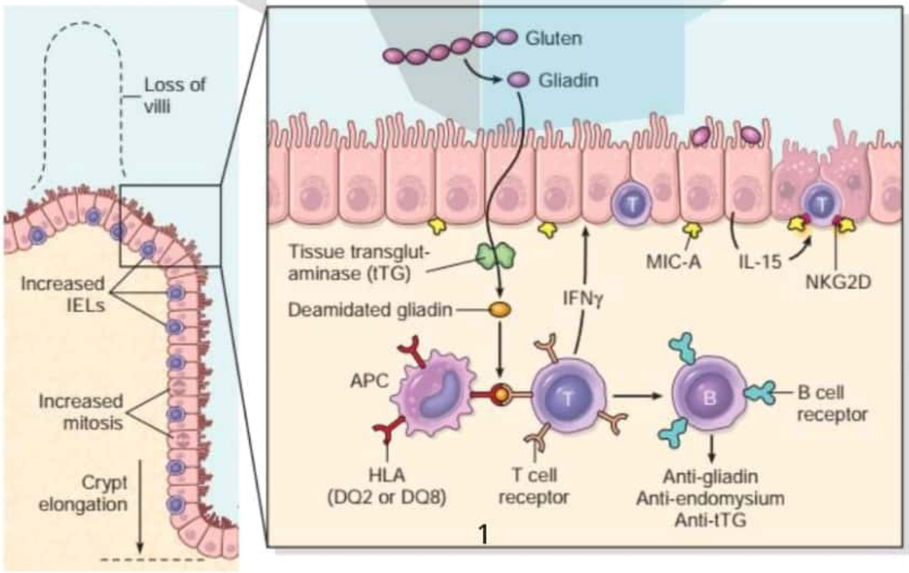
MALABSORPTION

Case: A chronic alcoholic patient presented with 8 months history of increased frequency of sticky stools 3-4 times/day. D-xylose test shows 5-hour urine excretion as 8g, Schilling test 5% urine excretion of cobalamin. Intestinal biopsy is normal. What is the most likely diagnosis?



- **Nutrients absorbed from**
  - Proximal SI : Fe, Ca, Mg, Cu, Zn, FA
  - Distal SI: Vit B12, Bile, Bilirubin

Biopsy findings of Malabsorption diseases

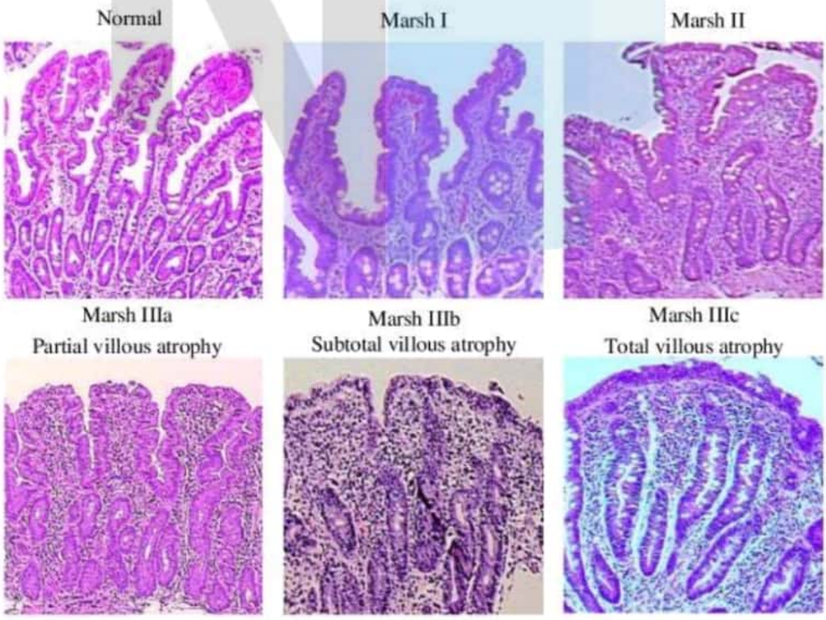


- **IEL (intraepithelial Lymphocytes)-** can lead to EATCL (Enteropathy associated T cell Lymphoma)

Modified Marsh Classification of histologic findings in celiac disease (Oberhuber)

MARSH TYPE	IEL / 100 ENTEROCYTES - JEJUNUM*	IEL / 100 ENTEROCYTES - DUODENUM*	CRYPT HYPERPLASIA	VILLI
0	<40	<30	Normal	Normal
1	>40	>30	Normal	Normal
2	>40	>30	Increased	Normal
3a	>40	>30	Increased	Mild atrophy
3b	>40	>30	Increased	Marked atrophy
3c	>40	>30	Increased	Complete atrophy

- Cutoff for IEL normally: Duodenum→ 30 ; Jejunum → 40
- First change: Increase in IEL
- Last change: Villous atrophy
- Normal Crypt : Villi Ratio is 1: 3



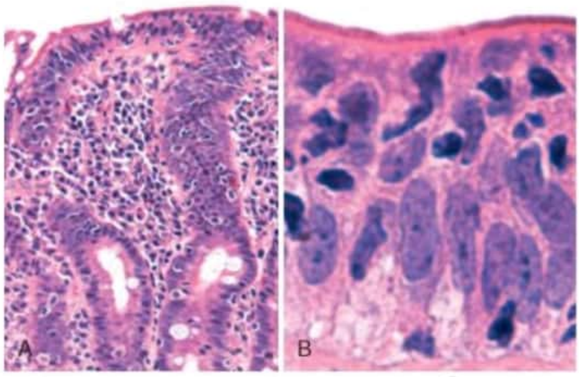
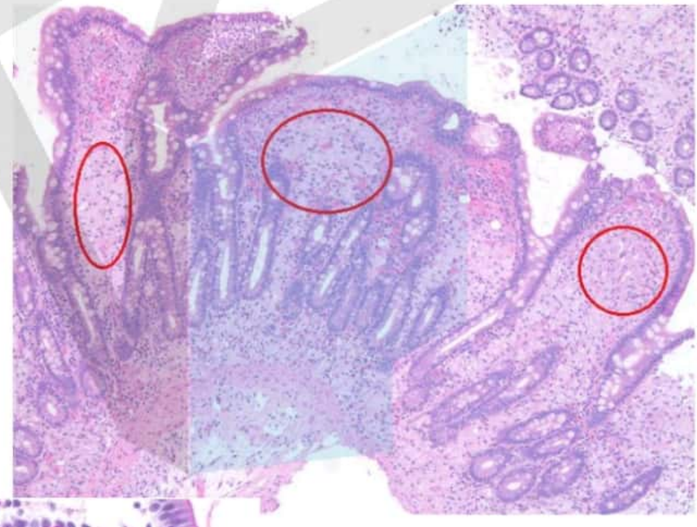


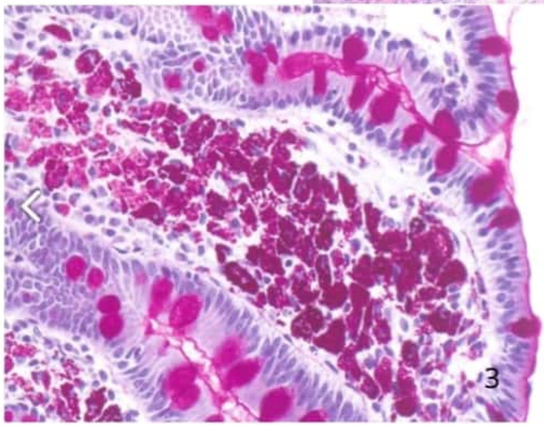
Figure 17.27 Celiac disease. (A) Advanced cases of celiac disease show complete loss of villi, or total villous atrophy. Note the dense plasma cell infiltrates in the lamina propria. (B) Infiltration of the surface epithelium by T lymphocytes, which can be recognized by their small, densely stained nuclei relative to larger, pale-staining epithelial nuclei.

Whipple's Disease

Circle: Areas of Foamy Macrophages in the submucosa

Special Stain for Whipple's Disease is PAS staining





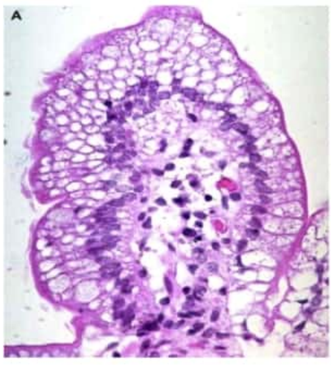
PAS positive diastase resistant material in submucosa in the MACROPHAGES.

This material is made of bacilli itself.

A-β Lipoproteinemia

Normal Villous.

Fat vacuoles are present in the epithelium



Disease	Intraluminal Digestion	Terminal Digestion	Transepithelial Transport	Lymphatic Transport
Celiac disease		+	+	
Environmental enteropathy		+	+	
Chronic pancreatitis	+			
Cystic fibrosis	+			
Primary bile acid malabsorption	+		+	
Carcinoid syndrome			+	
Autoimmune enteropathy		+	+	
Disaccharidase deficiency		+		
Whipple disease				+
Abetalipoproteinemia			+	
Viral gastroenteritis		+	+	
Bacterial gastroenteritis		+	+	
Parasitic gastroenteritis		+	+	
Inflammatory bowel disease	+	+	+	

"+" indicates that the process is abnormal in the disease indicated.

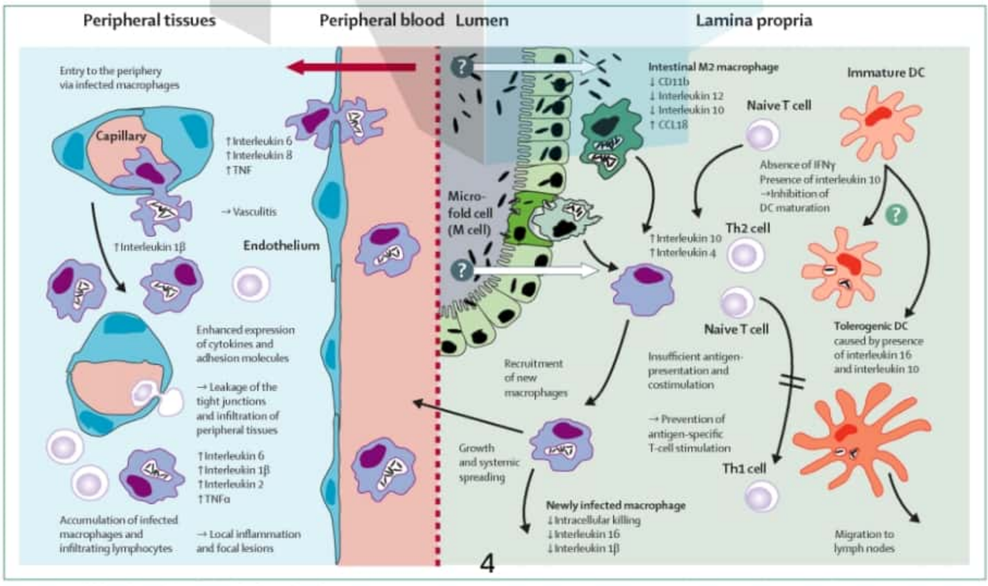
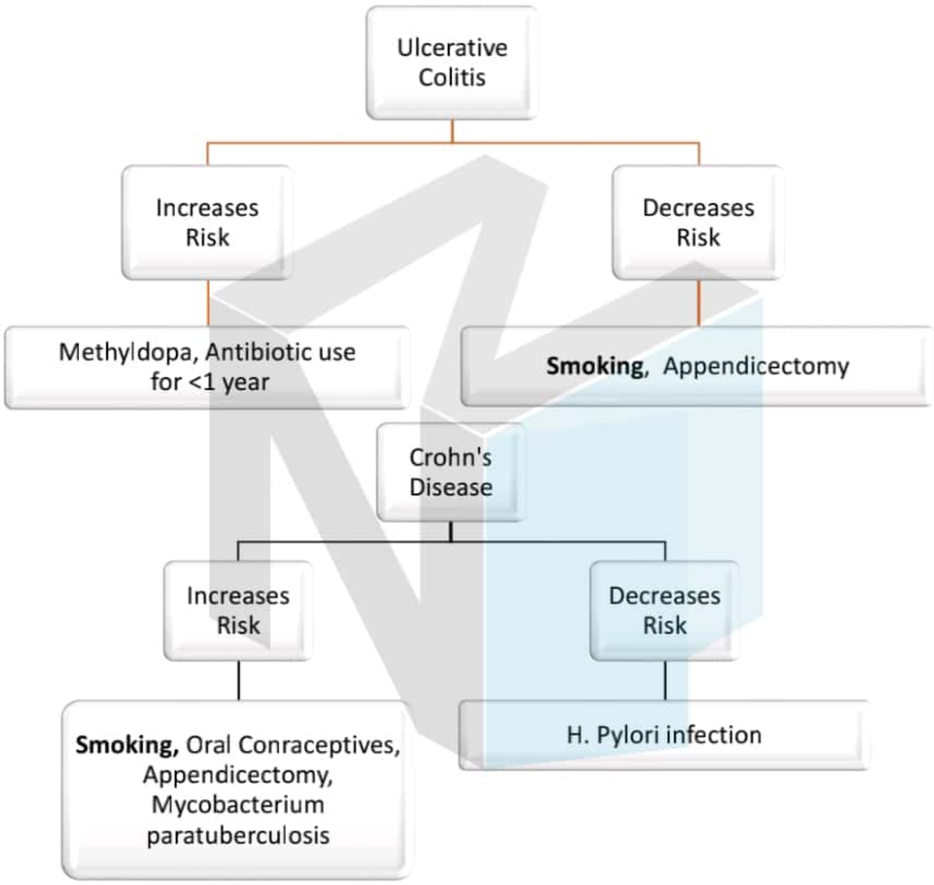


Figure 5: Model for the pathogenesis of Whipple's disease

INFLAMMATORY BOWEL DISEASE

Case: 25-year-old smoker presented with 6 months history of diarrhea and weight loss. On investigations Hb 10.0g/dL, Ferritin 8 µg/L, Anti tTG negative, Colonoscopy-severe ulceration in the terminal ileum, biopsies from the terminal ileum showed chronic inflammation with ulceration and granulomas. The most likely diagnosis is?



Clinical Features:

- UC: Tenesmus, Toxic Megacolon
- Crohn's Ds: Malabsorption, Fistula

INVESTIGATIONS

- Gold Standard: Biopsy
- P-ANCA: Ulcerative colitis (Non specific antibodies)
- ASCA: Crohn's disease (Non specific antibodies)

Biopsy Findings

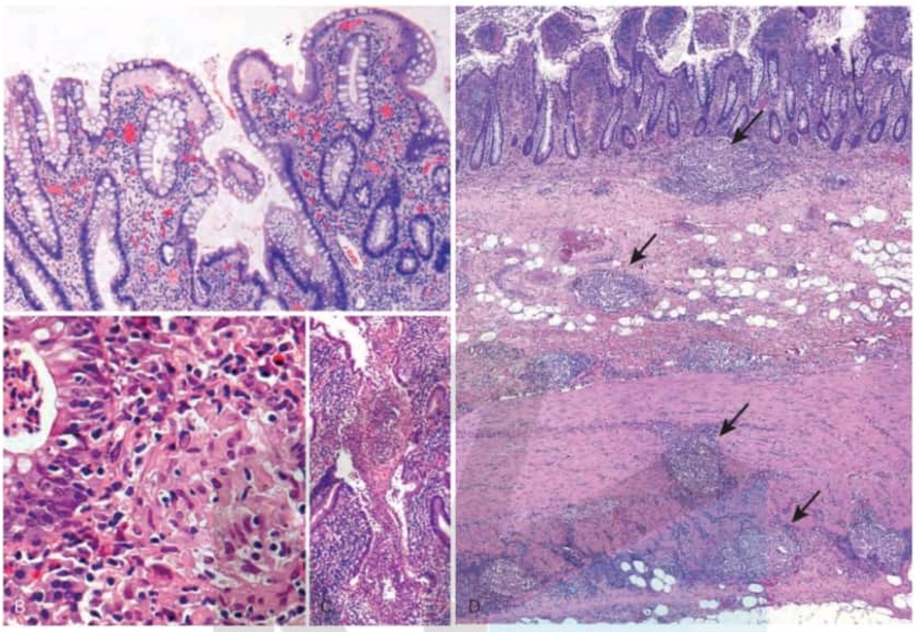


Figure 17.35 Microscopic pathology of Crohn disease. (A) Haphazard crypt organization results from repeated injury and regeneration. (B) Noncaseating granuloma. (C) Active Crohn disease, with ulceration and purulent exudate. (D) Transmural Crohn disease with submucosal and serosal granulomas *(arrows)*.

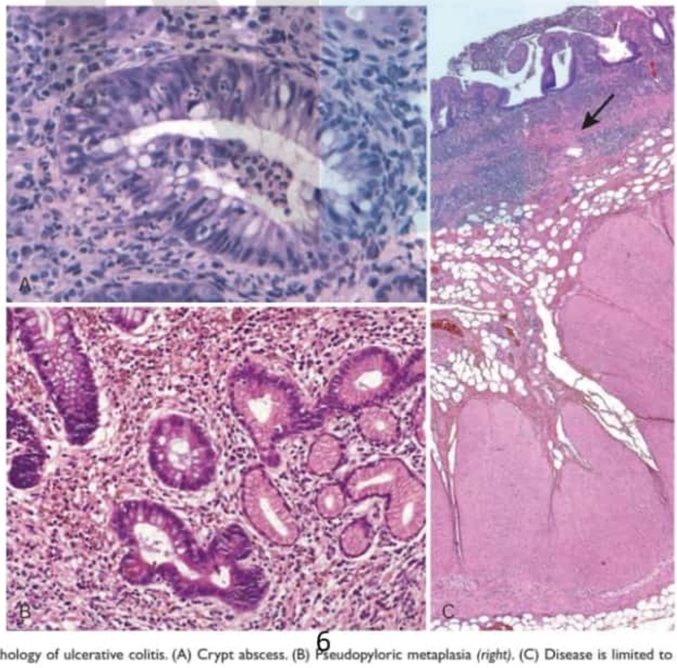
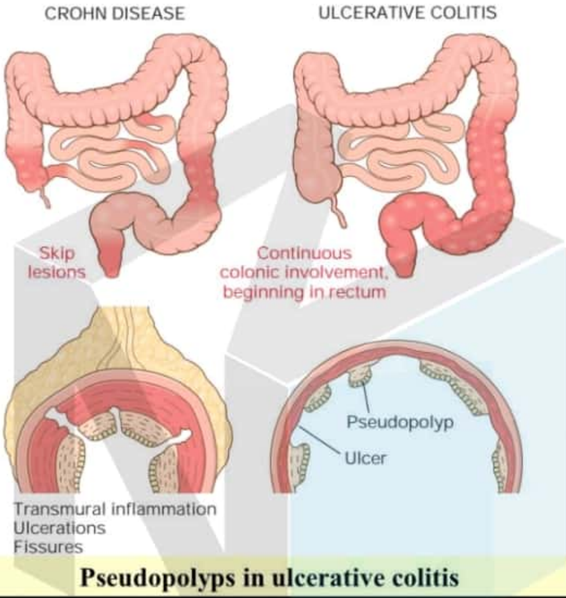
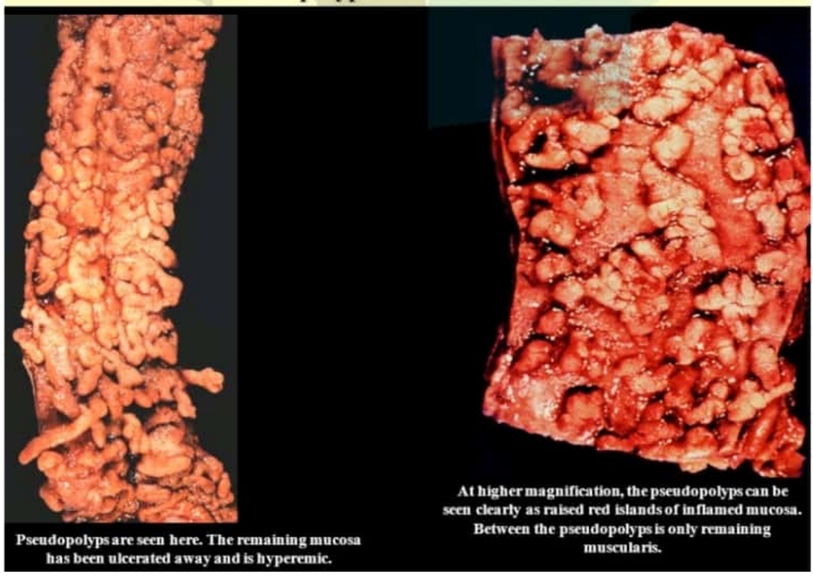


Figure 17.37 Histopathology of ulcerative colitis. (A) Crypt abscess. (B) Pseudopyloric metaplasia *(right)*. (C) Disease is limited to the mucosa

Crohn's Disease	Intestinal Tuberculosis
NON-Caseating Granuloma, Small Granuloma, Single granuloma (Non-coalescent) Trans-luminal Along full thickness of the GI wall Crypt abscess may be present LN are not involved	**Caseating** Granuloma, Large Granuloma, Coalescent Granuloma Only Sub-mucosa is involved commonly Crypt abscess is absent Lymph Nodes are involved Gold Std: PCR



Pseudopolyps in ulcerative colitis

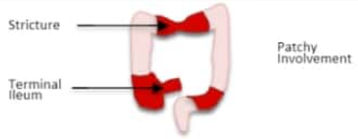


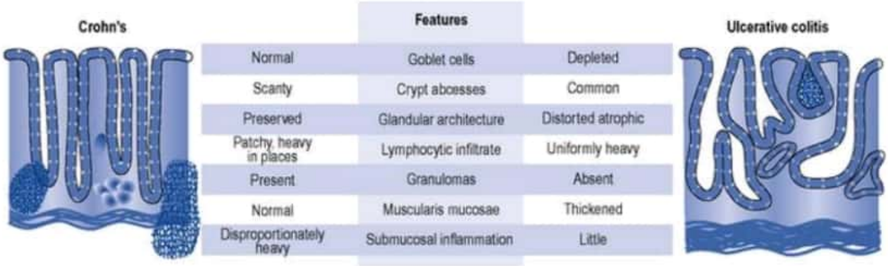
Pseudopolyps are seen here. The remaining mucosa has been ulcerated away and is hyperemic.

At higher magnification, the pseudopolyps can be seen clearly as raised red islands of inflamed mucosa. Between the pseudopolyps is only remaining muscularis.

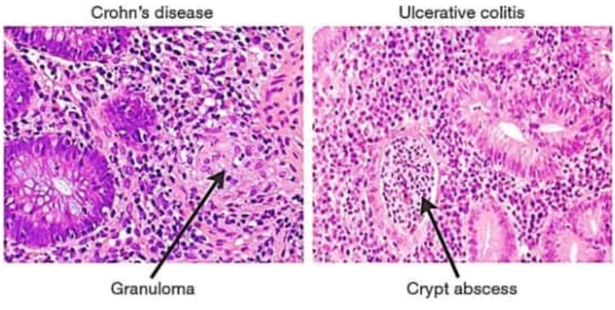
Inflammatory Bowl Disease
Group of chronic inflammatory disorders of the small and large intestines. Involves inflammation and ulceration.

Symptoms and Signs	Complications
• Frequent bowel movements • Diarrhea • Bloody stools • Abdominal pain • Urgency • Failure to thrive / weight loss	Toxic megacolon (more common UC)

	Ulcerative Collitis	Crohn's Disease
		
Location	• Always affects rectum extending to varying degrees around the large bowel	• Anywhere from the mouth to anus • Frequently affects the Terminal ileum Most cases (70-80%) have small bowel involvement and sparing of the rectum
Inflammation	Continuous, Diffuse mucosal inflammation (Inflammation limited to the mucosa) Sharp transition between diseased and normal colon	"Patchy (Skip areas), Transmural Inflammation" Locality in the setting of relatively normal intervening mucosa, segmental asymmetric involvement of different parts of the wall within given segments of bowel.
Clinical		
Hematochezia	common	rare
Mucus/Pus	common	rare
Small bowel disease	no	yes
UGI tract involvement	no	yes
Abdominal mass	rare	RLQ
Extra intestinal	common	common
Small bowel obstruction	no	common
colonic obstruction	rare	common
perianal disease	no	common
Strictures and Fistulas	no	yes
Pathology		
Structure	Thin bowel wall	Thick walled colon/SB, muscularis propria hypertrophy
Fat Wrapping	No	Yes
Cell Architecture	Numerous pseudopolyps or inflammatory polyps, Crypt distortion and abcess formation	less architectural distortion and mucin depletion
Granulomas	No	Yes
Lymphoid Aggregates	No	Yes



Feature	Crohn Disease	Ulcerative Colitis
Macroscopic		
Bowel region	Ileum ± colon	Colon only
Distribution	Skip lesions	Diffuse
Stricture	Yes	Rare
Wall appearance	Thick	Normal
Microscopic		
Inflammation	Transmural	Limited to mucosa
Pseudopolyps	Moderate	Marked
Ulcers	Deep, knife-like	Superficial, broad-based
Lymphoid reaction	Marked	Moderate
Fibrosis	Marked	Mild to none
Serositis	Marked	Mild to none
Granulomas	Yes (~35%)	No
Fistulae/sinuses	Yes	No
Clinical		
Perianal fistula	Yes (in colonic disease)	No
Fat/vitamin malabsorption	Yes	No
Malignant potential	With colonic involvement	Yes
Recurrence after surgery	Common	No
Toxic megacolon	No	Yes



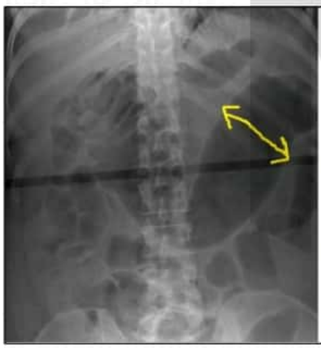
9

Radiology

LEAD PIPE SIGN: ULCERATIVE COLITIS

Frontal plain radiograph of the abdomen demonstrates a narrowed, featureless colon delineated with gas, with lack of haustral markings ➡ giving the lead pipe sign in ulcerative colitis.

Barium enema demonstrates barium delineating a narrowed, featureless colon with lack of haustral markings ➡ giving the lead pipe sign with tiny filling defects (pseudopolyps and granular mucosa).



Toxic Megacolon

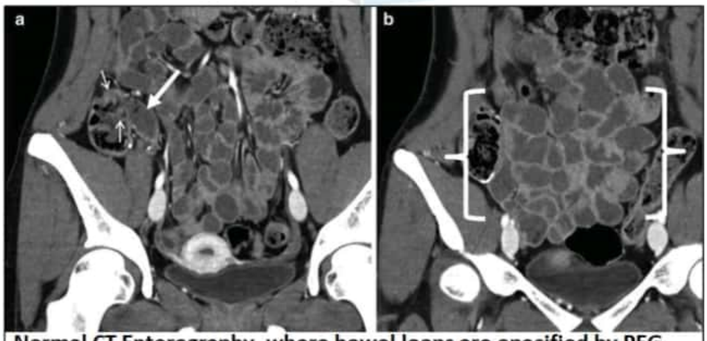
H/o IBD now c/o Acute abdomen

Diameter >6cms

Ahaustral

Differentiate from congenital megacolon (Hisrchsprung)

MR Enterography; Bowel loop opacification by Mannitol, done in places where radiation exposure is avoided. Eg- Bowel TB, Crohn's in children



Normal CT Enterography, where bowel loops are opacified by PEG IOC for Bowel TB and Crohn's Disease; can also show LN status

Ileo-caecal Koch's

Conical, Contracted, pulled up caecum with ileal stricture

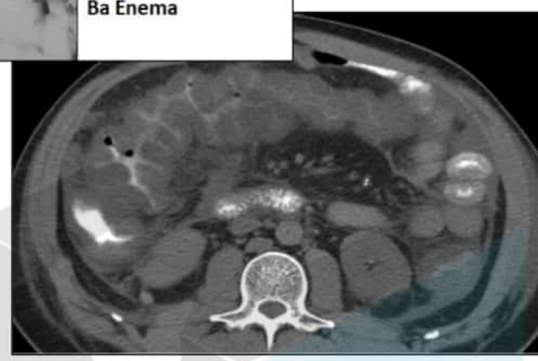
"Umbrella" or "Inverted Umbrella" Sign

Ba Enema

Hints for Crohn's Disease in a clinical question:

- **Perianal fistula**
- **Mesenteric border involvement**

(whereas in TB whole lumen is involved)

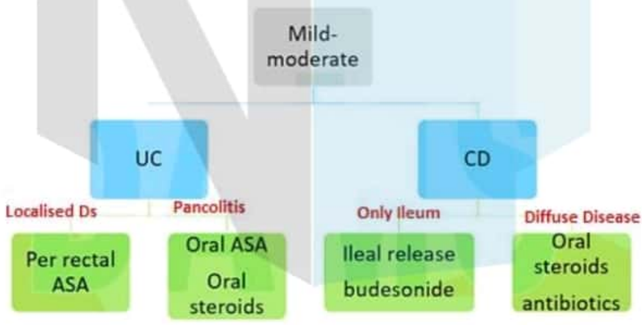


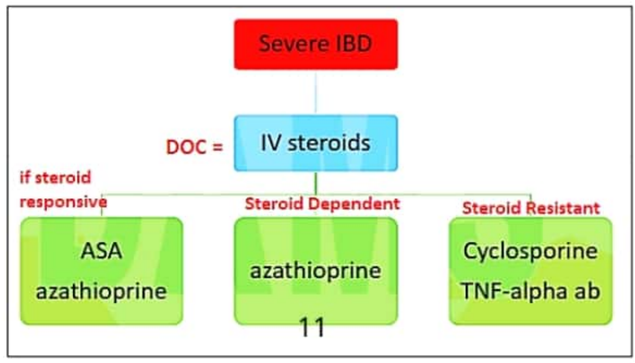
Pseudomembrane Enterocolitis on CT Scan

Edematous colonic wall indicated by sparse presence of Oral dye.

"Accordion Sign" on CT

Treatment





11

Irritable Bowel Syndrome

Case: A 28-year-old woman is presented with abdominal pain for more than 6 months the frequency of which has increased to 1 day per week for last 3months and pain is associated with defecation. There is hardening of stools since her symptoms have started. She has noted some mucus in the stool and mild bloating, but has not noted any blood in the stools. There is no fever, nocturnal diarrhea or weight loss. What is the likely diagnosis?

Symptoms favouring IBS	Symptoms against IBS
Age < 45 yrs	Fever
Mucus in stool	Blood in stools
Tenderness	Weight loss
Vomiting	Nocturnal Diarrhea

Rome IV Diagnostic Criteria for IBS-D

IBS—Recurrent abdominal pain on average at least 1 d/wk in the last 3 mo that is associated with at least 2 of the following criteria[a]:

1. Related to defecation
2. Associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool, with the IBS-D subtype identified with:
   >25% Bristol stool types 6 of 7 and
   <25% Bristol stool types 1 or 2

[a] Criteria fulfilled for the last 3 mo, with symptom onset at least 6 mo prior to diagnosis.

IBS-D, irritable bowel syndrome with predominant diarrhea

Treatment

- Initial recommendation is lifestyle and dietary modification (eg, exclusion of gas-producing and sugar rich foods) and a trial of psyllium in patients with IBS constipation (IBS-C).
- In patients who fail to respond to lifestyle and dietary modification and in patients with moderate to severe symptoms of IBS, drug therapy is used as an adjunctive treatment.
- Drug treatment is based on the predominant symptom i.e. constipation or diarrhoea.

Drugs given for IBS-constipation

1. Polyethylene Glycol(PEG): It is recommended in patients of IBS with constipation (IBS-C) who have failed a trial of soluble fiber (eg, psyllium/ispaghula). Other laxatives in the market are habit forming.

2. **Lubiprostone** : It is a locally acting chloride channel activator that enhances chloride-rich intestinal fluid secretion. Lubiprostone is used for treatment of IBS-C in women 18 years and older who have persistent constipation despite PEG. **HIGHLY TERATOGENIC**

3. **Guanylate cyclase agonists**: Linaclotide and plecanatide are guanylate cyclase agonists that stimulates intestinal fluid secretion and transit. ↑se in cGMP → Vasodilation→ Secretin. Given orally so that there is local effects. No side effects henceforth.

4. 5-HT4 receptor agonists: Agonists of the 5-HT4 receptor stimulate the release of

neurotransmitters and increase colonic motility. Tegaserod reduces abdominal pain in IBS as well as improves constipation.

5. Sodium/hydrogen exchanger 3 (NHE3) inhibitor: Tenapanor, a sodium/hydrogen exchanger 3 (NHE-3) reduces the absorption of sodium and phosphate and enhances intestinal fluid volume and transit.

Drugs given for IBS-diarrhoea

1. Mu receptor agonists:
a. Loperamide (pure mu receptor agonist) It use can lead to hard stools due to excessive water absorption.
b. Eluxadoline (mu-opioid receptor agonist and a delta-opioid receptor antagonist).

Delta receptor blocking action will increase intestinal secretion and hence stool remain soft.

2. Bile acid sequestrants: (cholestyramine, colestipol, colesevelam) – action in intestine lumen
• Bile acids cause diarrhea by stimulating colonic secretion and motility.
• Sequestrant of bile acids are used in patients with persistent diarrhea despite antidiarrheals treatment
• Gastrointestinal side effects including bloating, flatulence, abdominal discomfort, and constipation.

3. 5HT-3 receptor antagonists : Alosetron, a (5HT-3) antagonist, is approved for the treatment of severe diarrhea-predominant IBS in female patients whose symptoms have lasted for six months and who have failed to respond to all other conventional treatment.

Abdominal pain and bloating

1. Antispasmodic agents directly affect intestinal smooth muscle relaxation is mebeverine , and those that act via their anticholinergic properties are dicyclomine and hyoscine.
2. **Antidepressants** — Antidepressants have analgesic proper ties independent of their mood improving effects. TCAs have anticholinergic properties and slow down intestinal transit time, provide benefit in diarrhea-predominant IBS. For patients with IBS in whom depression is a cofactor, SSRIs/SNRIs (S/E is diarrhea) can also be used.

3. Other drugs in bloating: RIFAXIMIN, Probiotics

4. Antiemetics- Antiemetics are given to treat nausea and vomiting associated with IBS

Pseudomembranous Colitis

Case: A 40-year-old man presents with fever and diarrhea of 3 days duration. He recently completed a course of ampicillin for sore throat. Laboratory tests show a white blood cell count of 18000 /mm3. Which of the following is the most likely cause of this patient's diarrhea?

Diagnostic Criteria

(1) Diarrhea (≥3 unformed stools per 24 h for ≥2 days) with no other recognized cause and
(2) Detection of toxin A or B in the stool, detection of toxin producing C. difficile in the stool by nucleic acid amplification testing or by culture, or visualization of pseudo-membranes in the colon.

Severity Criteria

Severe CDI = TLC ≥15,000 cells/μL or creatinine level ≥1.5 times the premorbid value
Fulminant CDI = severe CDI + hypotension, shock, ileus, or toxic megacolon.

Investigations

TABLE 129-1 Relative Sensitivity and Specificity of Diagnostic Tests for *Clostridium difficile* Infection (CDI)

TYPE OF TEST	RELATIVE SENSITIVITY*	RELATIVE SPECIFICITY*	COMMENT
Stool culture for *C. difficile*	++++	+++	Most sensitive test; specificity of ++++ if the *C. difficile* isolate tests positive for toxin; turnaround time too slow for practical use
Cell culture cytotoxin test on stool	+++	++++	With clinical data, is diagnostic of CDI; highly specific but not as sensitive as stool culture; slow turnaround time
Enzyme immunoassay for toxins A and B in stool	++ to +++	+++	With clinical data, is diagnostic of CDI; rapid results, but not as sensitive as stool culture or cell culture cytotoxin test
Enzyme immunoassay for *C. difficile* common antigen in stool	+++ to ++++	+++	Detects glutamate dehydrogenase found in toxigenic and nontoxigenic strains of *C. difficile* and other stool organisms; more sensitive and less specific than enzyme immunoassay for toxins; requires confirmation with a toxin test; rapid results
Nucleic acid amplification tests for *C. difficile* toxin A or B gene in stool	++++	+++	Detects toxigenic *C. difficile* in stool; widely used in U.S. for clinical testing; more sensitive than enzyme immunoassay toxin testing; marked increase in CDI diagnoses when implemented
Colonoscopy or sigmoidoscopy	+	++++	Highly specific if pseudomembranes are seen; insensitive compared with other tests

Best investigation for CDI→ NAAT for C. difficile toxin
Most Sensitive Ix → Stool Culture
Most Specific → Colonoscopy

Treatment

Initial Infection

Non severe disease (Mild & Moderate) White blood cell count ≤15,000 cells/mL and serum creatinine <1.5 mg/dL	Oral Vancomycin (Bacteriostatic) - **DOC** OR Oral Fidaxomicin (Bactericidal) If above agents are unavailable: Metronidazole Treatment is given for 10 days

Severe disease (White blood cell count >15,000 cells/mL and/or serum creatinine ≥1.5 mg/dL)	Oral Vancomycin OR Oral Fidaxomicin NO ROLE OF METRONIDAZOLE Treatment is given for 10 days
Fulminant disease (severe complicated infection) Hypotension or shock, ileus, megacolon	Enteric vancomycin plus parenteral metronidazole (Oral/NG Tube) If ileus is present, rectal vancomycin may be administered as a retention enema

Recurrent Infection

First recurrence (non severe and severe disease)	If vancomycin was used for the initial episode: Vancomycin pulsed-tapered regimen **OR** Fidaxomicin If fidaxomicin or metronidazole was used for the initial episode: Vancomycin
Second recurrence (non severe and severe disease)	Vancomycin pulsed-tapered regimen **OR** Fidaxomicin **OR** Vancomycin followed by oral rifaximin
Third or subsequent recurrence (≥3) (non severe and severe disease)	For at least three CDI episodes (ie, initial episode plus two recurrences) of CDI with received appropriate antibiotic treatment , **Fecal Microbiota Transplantation (FMT)** is recommended

INFECTION PREVENTION

- Minimizing antibiotic use(clindamycin, broad spectrum beta lactams)
- Avoiding gastric acid suppression
- Primary & secondary prophylaxis with oral vancomycin may be of benefit in patients at high risk for CDI.
- Metronidazole should not be used for secondary prophylaxis because of its dose-dependent association with peripheral neuropathy.
- Adjunctive use of monoclonal antibodies i.e Bezlotoxumab (a monoclonal antibody that binds to *C. difficile* toxin B) may reduce the recurrence rate of infection.

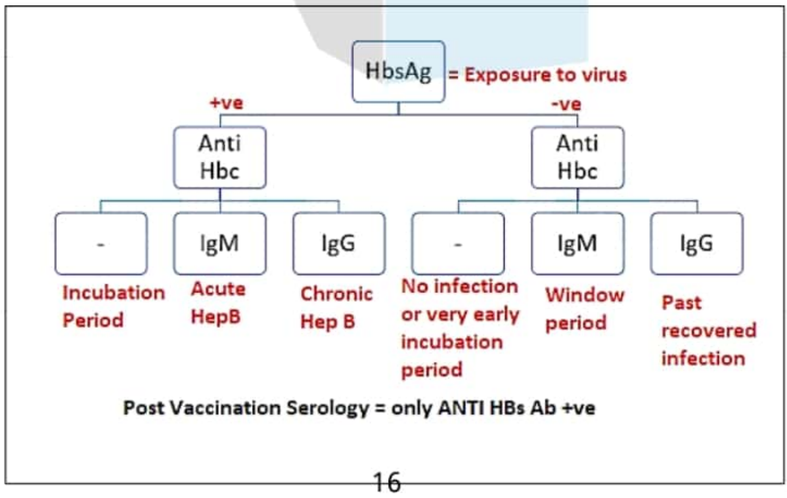
Max risk is with CLINDAMYCIN

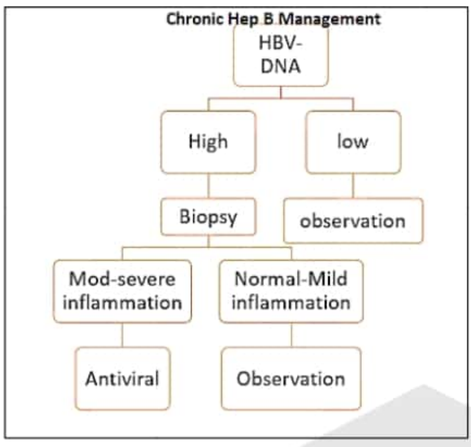
Careless PPI administration

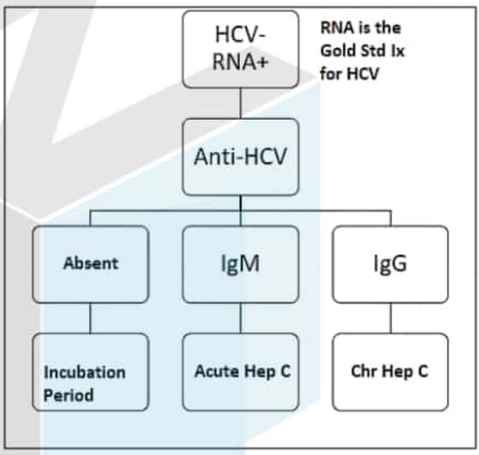
Acute Hepatitis

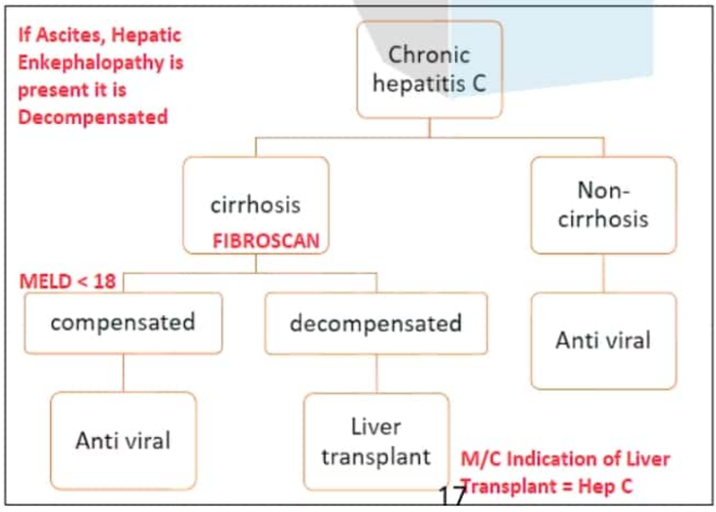
Case: A 60-year-old man presented with nausea and itching. A careful history elicits that he recently celebrated his wedding anniversary on a cruise ship from which they returned a few weeks ago. He has recently noted dark urine and pale stool. His wife is not unwell but she is vegetarian and he mentions he ate large amounts from the seafood buffet. He has no other risk factors for jaundice. His LFTs confirm he is jaundiced with an acute hepatitis.

- Hepatitis A
  - Mode of transmission: Feco-Oral route
  - MC Cause of Acute Viral Hepatitis in Children
  - Relapsing Hepatitis
- Hepatitis E
  - Mode of transmission: Feco-Oral route (Still does not get transmitted to close contact)
  - MC Cause of Acute Viral Hepatitis in Adults
  - Cholestatic Hepatitis
- Hepatitis B
  - Mode of transmission: Vertical (M/C) , Sexual, percutaneous
  - M/C Cause of Blood Transfusion related virus
  - M/C Cause of HCC
  - M/C Viral Cause of Viral hepatitis
  - M/C Cause of Carrier state
- Hepatitis C
  - Mode of transmission: percutaneous
  - M/C Viral Cause of Cirrhosis
  - Max risk of chronic hepatitis




Chronic Hep B Management
HBV-DNA
High
low
Biopsy
observation
Mod-severe inflammation
Normal-Mild inflammation
Antiviral
Observation


HCV-RNA+
RNA is the Gold Std Ix for HCV
Anti-HCV
Absent
IgM
IgG
Incubation Period
Acute Hep C
Chr Hep C


If Ascites, Hepatic Enkephalopathy is present it is Decompensated
Chronic hepatitis C
cirrhosis
FIBROSCAN
Non-cirrhosis
MELD < 18
compensated
decompensated
Anti viral
Anti viral
Liver transplant
M/C Indication of Liver Transplant = Hep C

- **Hepatitis D**
  - Mode of transmission: Close contact (endemic) or percutaneous (nonendemic)
  - Inhibits Hep B replication
  - Max risk of fulminant hepatitis

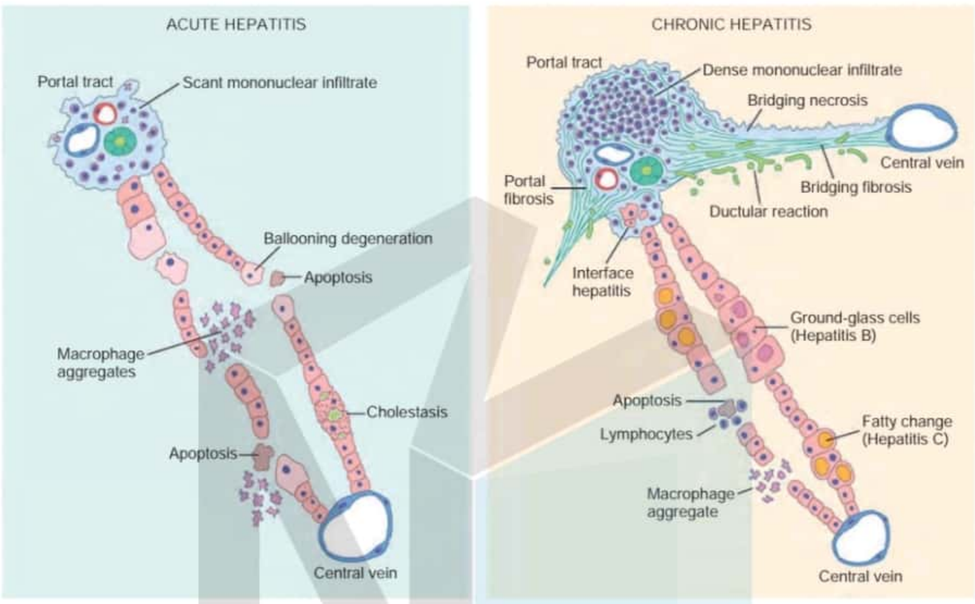


Figure 18.13 Diagrammatic representation of the morphologic features of acute and chronic hepatitis. Acute hepatitis is characterized by lobular inflammation and hepatocellular injury, and chronic hepatitis shows dense portal inflammation. Bridging necrosis can occur in severe acute hepatitis, and fibrosis is seen in chronic hepatitis. Ductular reaction is often present in areas of fibrosis in chronic hepatitis.

Q. Interface hepatitis (aka Piecemeal Necrosis) is the most important sign of Chronic hepatitis

Q. Acute Hepatitis- Scant Mononuclear infiltrates in the portal tract

Q. Chronic Hepatitis- Dense Mononuclear infiltrates in the portal tract

Q Hep B- Ground glass cells , Hep C- Fatty Change

Q Councilman bodies more specific for acute hepatitis

Q Ground glass hepatocytes contain Hep B surface antigen

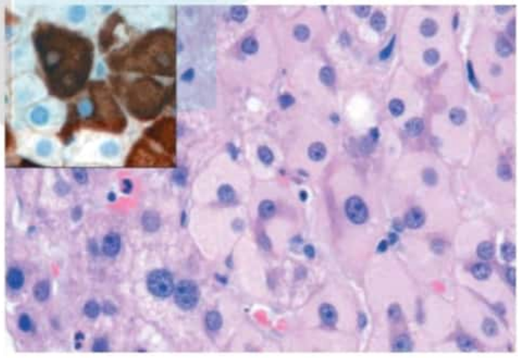
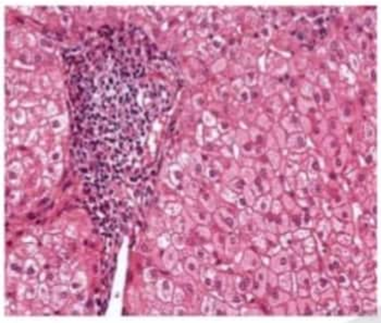
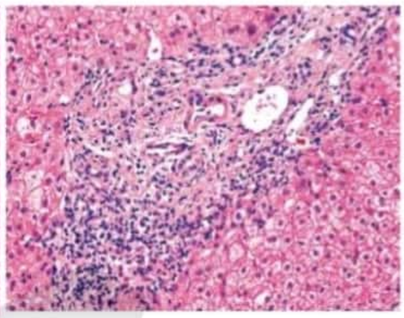


Figure 18.14 Ground-glass hepatocytes in chronic hepatitis B caused by accumulation of hepatitis B surface antigen in the endoplasmic reticulum. The cytoplasmic inclusions are light pink and finely granular on hematoxylin and eosin staining; immunostaining *(inset)* confirms that they contain hepatitis B surface antigen *(brown)*.

Chronic hepatitis



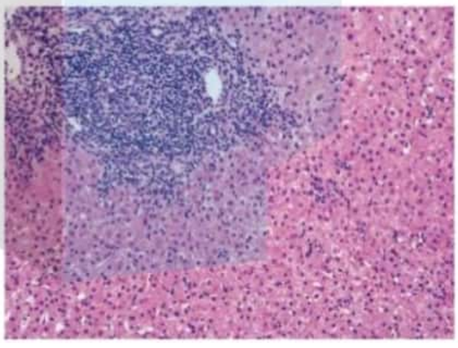
The portal tract is heavily infiltrated with lymphocytes (H&E)



Interface hepatitis-process of inflammation and erosion of the hepatic parenchyma at its junction with portal tracts or fibrous septa (H&E)

Chronic hepatitis C

- The portal tract is heavily infiltrated by lymphocytes,
- A **lymphoid follicle with germinal center** has formed
- 15-25% may have steatosis

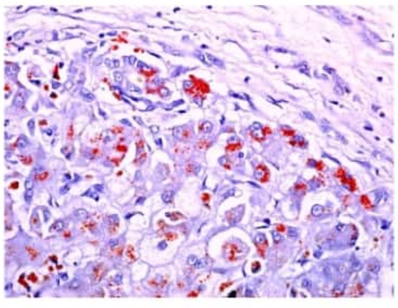


WILSON's Disease

Special Stains for Copper-

1. RHODAMINE Stain (Image) : Red colour shows intracellular copper in corneal cells.

2. Orcein



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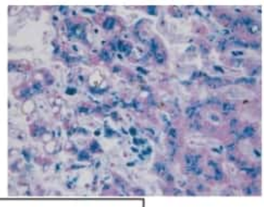
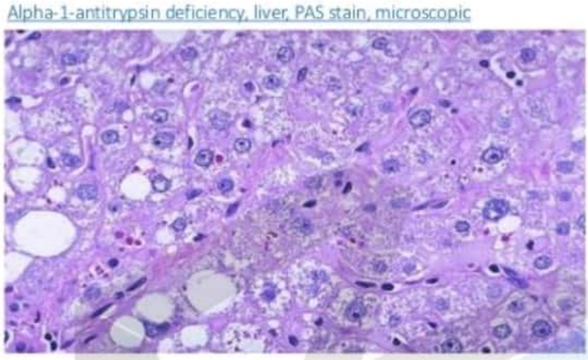
Hemochromatosis

Special Stain: Prussian Blue Stain specific for iron.



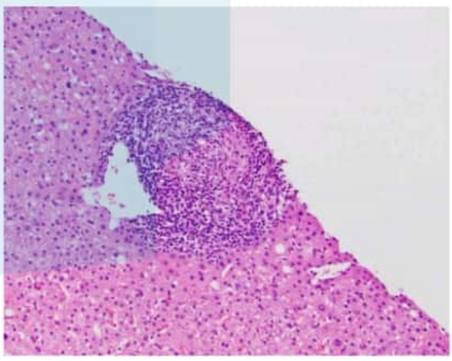
Alpha-1-antitrypsin deficiency, liver, PAS stain, microscopic



- The periportal red hyaline globules seen here with periodic acid-Schiff (PAS) stain are characteristic for alpha-1-antitrypsin (AAT) deficiency. The globules are collections of alpha-1-antitrypsin not being excreted from hepatocytes. This may eventually lead to chronic hepatitis and cirrhosis.

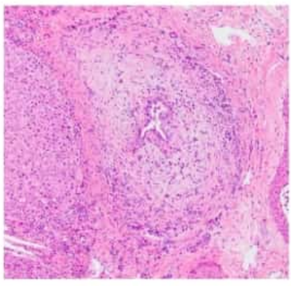
Primary Biliary Cirrhosis

- Key finding is the **florid duct lesion:** interlobular bile ducts (within small portal tracts) are destroyed by poorly formed portal epithelioid granulomas
- Dense lymphocytic infiltrate in portal tracts can also be seen, mimicking hepatitis

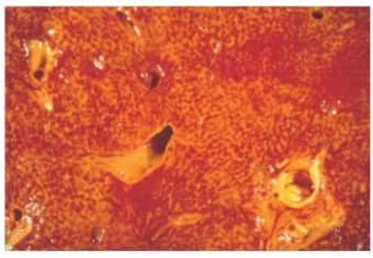


Primary Sclerosing Cholangitis

Periductal "onion skin" fibrosis surrounding an injured but intact bile duct in a liver transplanted for primary sclerosing cholangitis

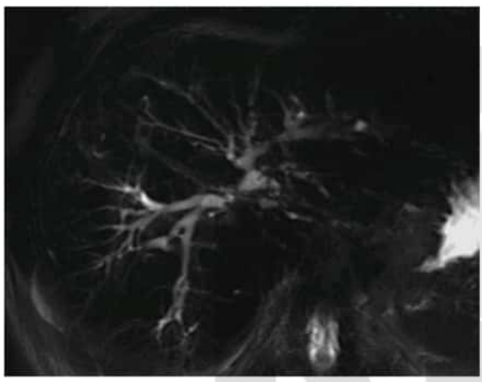


CVC Liver



Congestive hepatopathy, also known as nutmeg liver and chronic passive congestion of the liver, is liver dysfunction due to venous congestion, usually due to congestive heart failure.

The gross pathological appearance of a liver affected by chronic passive congestion is "speckled" like a grated nutmeg kernel; the dark spots represent the dilated and congested hepatic venules and small hepatic veins. The paler areas are unaffected surrounding liver tissue.



MRCP in Primary Sclerosing Cholangitis

The entire biliary tree (both intra and extrahepatic) may be involved, with multiple strictures scattered along its length.

Treatment for HEPATITIS B VIRUS

1. Pegylated Interferon alpha-2a

- Interferon is used primarily in treatment of young adult patients with well compensated liver disease who do not wish to be on long-term treatment.
- Interferon alfa is administered by subcutaneous injection for fix 48-52 weeks
- The advantages of interferon compared to nucleos(t)ide analogues are its finite duration of treatment, the absence of selection of resistant variants, and a more durable response.
- Adverse reactions (>40%): fatigue/asthenia, pyrexia, myalgia, and headache
- May cause fatal neuropsychiatric, autoimmune and infectious disorders
- Frequent hematologic monitoring required
- Contraindicated in advanced liver disease and in pregnancy

2. Nucleos(t)ide analogues

- DNA polymerase inhibitors
- Nowadays preferred drugs for the treatment of hepatitis B treatment naive patient
- Drugs are given by oral route
- Can be given for indefinite time
- Preferred over interferon alpha in patient of cirrhosis and in pregnancy
- Tenofovir, lamivudine and emtricitabine are also used to treat HIV

A. Tenofovir (most preferred) (can be given as Oral Monotherapy)
Available in two forms :
Tenofovir alafenamide (preferred in non pregnant, less renal toxicity and osteoporosis)
Tenofovir disoproxil fumarate (preferred in pregnant, more clinical experience)
- Approved for individuals ≥ 2 years old
- Indefinite treatment for patients with cirrhosis
- Dose reduction in renal impairment

B. Entecavir (can be given as Oral Monotherapy)
- Almost same properties and efficacy as tenofovir
- Take on an empty stomach
- Monitor for lactic acidosis in decompensated cirrhosis.

C. Adefovir, Lamivudine, Telbivudine
- Alternative agents due to high incidence of HBV resistance with monotherapy
- Dose adjust for renal impairment
- Abrupt discontinuation causes hepatitis flares

Treatment for HEPATITIS C VIRUS

1. Directly acting antiviral (DAA)

A. Protease inhibitors (inhibitor of HCV NS3 protease) (suffix- previr)
- Simeprevir
- Paritaprevir
- Grazoprevir
- Asunaprevir

B. Direct protein inhibitors (inhibitor of HCV NS5A protein) (suffix-asvir)
- Velpatasvir
- Ombitasvir
- Daclatasvir
- Ledipasvir

C. Nucleotide Polymerase inhibitor: (inhibitors of HCV NS5B) (suffix- buvir)
- Sofosbuvir
- Dasabuvir

- Treatment is given by oral route for 12-weeks therapy in patients without cirrhosis and 24-week therapy in patients with cirrhosis
- Oral Route and given in combination.
- DAA associated with many drug interaction with liver enzyme and p-glycoprotein inducers and inhibitors.
- Co administration of sofosbuvir and amiodarone may cause severe bradycardia and fatal cardiac arrest
- Avoid sofosbuvir if CrCl < 30 mL/min

- Simeprevir is contraindicated in decompensated cirrhosis
- Grazoprevir/elbasvir regimen is preferred treatment in renal impairment patients
- Ledipasvir and velpatasvir absorption requires acid gastric pH

2. Interferon & Ribavirin

- For patients who are treated with a regimen that contains peginterferon and ribavirin, side effects can be substantial.
- These most commonly are flu-like symptoms, fatigue, neuropsychiatric symptoms, and hematologic effects.
- Patients should thus be evaluated regularly for toxicity during the course of therapy with such regimens.